AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for identifying a drug candidate for promoting tissue-specific differentiation of a naïve embryonic stem cell, the method comprising the steps of:

(A) providing a library of test substances, the library comprising at least a first test substance and a second test substance, the first and second test substances having different molecular structures;

(B) providing an *in vitro* culture of stem cells, the culture being divided into at least a first subculture and a second subculture and the stem cell cultures;

(C) culturing the stem cells for at least about 3 days in the absence of a test substance;

~~(C)~~ (D) contacting the first subculture with the first test substance and the second subculture with the second test substance;

~~(D)~~ (E) culturing for at least about 14 days, the first and second subcultures respectively contacted with the first and second test substances under conditions that would promote tissue-specific differentiation of the stem cells if an agent that promoted tissue-specific differentiation was in contact with the stem cells; and

~~(E)~~ (F) analyzing the cells in the first and second subcultures for increased tissue-specific gene expression.

2. (Original). The method of claim 1, wherein the stem cells are embryonic stem cells.

3. (Original) The method of claim 2, wherein the embryonic stem cells are mammalian embryonic stems cells.

4. (Previously Amended) The method of claim 3, wherein the mammalian embryonic stem cells are murine embryonic stem cells.

5. (Previously Amended) The method of claim 4, wherein the murine embryonic stem cells are R1 embryonic stem cells.

6. (Previously Amended) The method of claim 3, wherein the mammalian embryonic stem cells are human embryonic stem cells.

7. (Cancelled)

8. (Currently Amended) The method of claim 1, wherein the conditions that would promote tissue-specific differentiation of the stem cells comprises culturing the first and second subcultures at about 37°C <u>in a humidified, carbon-dioxide containing incubator</u>.

9. (Cancelled).

10. (Original) The method of claim 1, wherein the conditions that would promote tissue-specific differentiation of the stem cells comprises culturing the first and second subcultures for a time period of at least five days.

11. (Original) The method of claim 10, wherein the time period is at least seven days.

12. (Original) The method of claim 11, wherein the time period is between seven and eighteen days.

13. (Original) The method of claim 1, wherein the first and second subcultures are cultured in a microtiter plate.

14. (Currently Amended) The method of claim 1, wherein the step ~~(E)~~ (F) of analyzing the cells in the first and second subcultures for increased tissue-specific gene expression comprises isolating mRNA from the first and second subcultures.

15. (Original) The method of claim 14, wherein total cellular RNA is isolated from the first and second subcultures.

16. (Currently Amended) The method of claim 14, wherein the step ~~(E)~~ (F) further comprises reverse-transcribing the mRNA to create cDNA.

17. (Currently Amended) The method of claim 1, wherein the step ~~(E)~~ (F)of analyzing the cells in the first and second subcultures for increased tissue-specific gene expression comprises performing a polymerase chain reaction (PCR).

18. (Original) The method of claim 14, wherein the isolated mRNA is immobilized on a substrate.

19. (Original) The method of claim 18, wherein the substrate is contacted with a probe that specifically hybridizes to the tissue-specific mRNA.

20. (Currently Amended) The method of claim 1, wherein the step ~~(E)~~ (F) of analyzing the cells in the first and second subcultures for increased tissue-specific gene expression is performed using gene chip technology.